

In the Claims

This listing of claims will replace all prior versions and listings of claims in this application.

1 (currently amended). A method for the identification and/or quantification of one or more proteins derived from the proteome of a cell in a sample containing a mixture of such proteins, wherein said method comprises the steps of:

- a) providing a sample which contains a mixture of proteins;
- b) providing a reagent for the analysis of peptides wherein the reagent has the general formula

A-Y-PRG

in which

A constitutes at least one functional group for the reversible, covalent or non-covalent binding to a support material,

Y is a group comprising at least one chelate function for metals ~~being low in isotopes~~, and comprising a metal ion bound thereto wherein the metal is selected from the group consisting of Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La, Li, Lu, Mn, Na, Nd, Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tm, V, W, Y, Yb and Zn; and Zn;

PRG is a reactive group for the selective binding to peptides or other biomolecules to be analyzed;

- c) chemically or proteolytically cleaving the proteins in the sample in order to produce peptides;
- d) coupling the peptides to the reagent of step b);
- e) selecting the peptides labeled in step d) using a functional group for the reversible, covalent or non-covalent binding to a support material and removal of unbound peptides;
- f) releasing the bound peptides from the support material and elution from the matrix; and
- g) detecting and identifying the labeled peptides by means of mass spectrometry.

2 (currently amended). The method, according to claim 1, wherein the cleavage of the peptides is performed enzymatically by a proteolytic enzyme.

3 (previously presented). The method, according to claim 1, wherein the labeled peptides, after their release from the support material and before their analysis by mass spectrometry, are separated from each other by means of HPLC.

4 (previously presented). The method, according to claim 1, characterized in that several protein- and/or peptide-containing samples are analyzed together.

5 (previously presented). The method, according to claim 1, further comprising the sequencing of the labeled peptides.

6 (currently amended). A method for the detection of the relative expression of proteins in a protein-containing sample, wherein said method comprises the steps of:

- a) providing a biological sample which contains proteins;
- b) providing a reagent for the analysis of peptides wherein the reagent has the general formula

A-Y-PRG

in which

A constitutes at least one functional group for the reversible, covalent or non-covalent binding to a support material,

Y is a group comprising at least one chelate function for metals being low in isotopes, and comprising a metal ion bound thereto wherein the metal is selected from the group consisting of Ag, Al, As, Au, Be, Cd, Ce, Co, Cr, Cu, Dy, Er, Eu, Fe, Gd, Hg, Ho, In, La, Li, Lu, Mn, Na, Nd, Ni, Pb, Pr, Rb, Rd, Sb, Sm, Sn, Tb, Tl, Tm, V, W, Y, Yb and Zn and Zn-, and

PRG is a reactive group for the selective binding to peptides or other biomolecules to be analyzed and said reagent contains no isotopes;

- c) chemically or proteolytically cleaving the proteins in the sample in order to produce

peptides;

- d) coupling the peptides to the reagent of step b);
- e) selecting the peptides labeled in step d) utilizing a functional group for the reversible, covalent or non-covalent binding to a support material and removal of the unbound peptides;
- f) releasing the bound peptides from the support material and elution from the matrix;
- g) detecting and identifying the labeled peptides by means of mass spectrometry; and
- h) measuring the relative occurrence of the differently labeled peptides as distinct peaks of ions in order to determine the relative expression of the protein, from which the affinity-labeled peptide is derived.

7 (previously presented). The method, according to claim 6, characterized in that the arrangement of the groups A, Y and PRG is interchanged.

8 (previously presented). The method, according to claim 6, characterized in that the labeled peptides are detected by means of a tandem technique selected from the group consisting of matrix-assisted laser desorption/ionization (MALDI), time-of-flight (TOF)-TOF-MS and electrospray ionization (ESI)-MS.

9-21 (cancelled).

22 (new). The method according to claim 1, wherein said mixture of proteins has not been labeled with an isotope.

23 (new). The method according to claim 1, wherein the arrangement of the groups A, Y and PRG is interchanged.

24 (new). The method according to claim 1, wherein the PRG group is selected from the group consisting of sulphydryl-reactive groups, amine-reactive groups and enzyme substrates.

25 (new). The method according to claim 24, wherein the PRG group is selected from the group consisting of amine-reactive pentafluorophenyl ester groups, amine-reactive N-hydroxysuccinimide ester groups, sulfonylhalides, isocyanates, isothiocyanates, active esters, tetrafluorophenyl esters, acid halides, acid anhydrides, homoserine lactone-reactive primary amine groups, carboxylic acid-reactive amines, alcohols, 2,3,5,6-tetrafluorophenyltrifluoro-acetates, iodine acetyl amide groups, epoxides, α -haloacyl groups, nitriles, sulfonated alkyls, arylthiols and maleimides.

26 (new). The method according to claim 1, wherein A is selected from the group consisting of biotin, modified biotin, 1,2-diols, glutathiones, maltoses, nitrilotriacetic acid groups, oligohistidines and haptens.

27 (new). The method according to claim 1, further comprising a linker between the groups A, Y and/or PRG that is cleavable.

28 (new). The method according to claim 27, wherein the linker contains a disulfide group.

29 (new). The method according to claim 6, wherein said mixture of proteins has not been labeled with an isotope.

30 (new). The method according to claim 6, wherein the PRG group is selected from the group consisting of sulphydryl-reactive groups, amine-reactive groups and enzyme substrates.

31 (new). The method according to claim 30, wherein the PRG group is selected from the group consisting of amine-reactive pentafluorophenyl ester groups, amine-reactive N-hydroxysuccinimide ester groups, sulfonylhalides, isocyanates, isothiocyanates, active esters, tetrafluorophenyl esters, acid halides, acid anhydrides, homoserine lactone-reactive primary amine groups, carboxylic acid-reactive amines, alcohols, 2,3,5,6-tetrafluorophenyltrifluoro-acetates, iodine

acetylamide groups, epoxides, α -haloacyl groups, nitriles, sulfonateds alkyls, arylthiols and maleimides.

32 (new). The method according to claim 6, wherein A is selected from the group consisting of biotin, modified biotin, 1,2-diols, glutathiones, maltoses, nitrilotriacetic acid groups, oligohistidines and haptens.

33 (new). The method according to claim 6, further comprising a linker between the groups A, Y and/or PRG that is cleavable.

34 (new). The method according to claim 33, wherein the linker contains a disulfide group.